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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/254,529	08/04/1999	SUSAN MARY KINGSMAN	9192.9USWO	7151

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EXAMINER
KAUSHAL, SUMESH

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 11/06/2002 19

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/254,529	KINGSMAN ET AL.	
	Examiner	Art Unit	
	Sumesh Kaushal Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 August 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) *24, 32-33, 36, 38, 40-43* is/are allowed.

6)☒ Claim(s) *26-31,35 and 39* is/are rejected.

7)☐ Claim(s) *25,34 and 37* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's response filed on 08/23/02 has been acknowledged.

Claims 42-43 are newly filed.
Claims 24, 26-34, 37, 40-41 are amended.
Claims 24-43 were pending and were examined in this office action.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The references cited herein are of record in a prior Office action.

► *If the claims are amended, added and/or canceled in response to this office action the applicants are required to follow Amendment Practice under 37 CFR § 1.121 (http://www.uspto.gov) and A CLEAN COPY OF **ALL** PENDING CLAIMS IS REQUESTED.*

Claim Rejections - 35 U.S.C. § 112

Claim 28 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a retroviral particle encoding a nucleotide sequence of interest, does not reasonably provide enablement for a retroviral particle that encodes a therapeutic gene. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to the invention **commensurate in scope** with these claims for the same reasons of record as set forth in the earlier official action mailed on Paper No.16, 03/12/02.

Citing recently published articles the applicant argues that it is now evident ~~now~~ that gene therapy works (response, page 7, para.4). The applicant further argues that vector carrying the therapeutic gene (NS) is considered a therapeutic tool for the selection of target cells expressing the therapeutic protein (response, page 7, para.5). The applicant concluded that invention as claimed by the instant specification.

However, this is not found persuasive because applicant's argument alone cannot take place of evidence lacking in the record (see In re Scarbrough 182 USPQ, (CCPA) 1979). The scope of the claims must bear a reasonable correlation with the scope of enablement (In re

Fisher, 166 USPQ 19 24 (CCPA 1970)). Invention as claimed recites "therapeutic gene" which is a statement of intended use in gene therapy. The instant specification fails to disclose a single working example that establishes the treatment of a disease or disorder by delivering a therapeutic gene of interest to a target site in vivo via any and all routes of administration. The earlier office action provides evidence that the gene therapy is considered highly experimental area of research at this time, and both researchers and the public agree that demonstrable progress to date has fallen short of initial expectations (Anderson WF, Nature 392:25-30, 1998). None of the human studies to date has shown definite efficacy, despite more than 300 protocols involving 3000 patients since September 1990 (Anderson page 25 col.1 para.1). Most studies have neglected to include well-defined biochemical or clinical end points that would clearly indicate whether the therapy is having a desired effect. In instant case, considering the scope of therapeutic gene (as claimed), it is unclear whether the disease would be the result of the loss of gene product or is the result of altered gene product function. It is even unclear whether the treatment of the disease associated with the gene (as claimed) would require increase or decrease in the expression of the gene product. Therefore the identification of a particular gene product and its well-defined biochemical or clinical end points are considered germane to the gene bases therapeutics.

Since the gene based therapies are not routine in the art and without sufficient guidance to a specific therapeutic gene the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). It is noted that the unpredictability of a particular area may alone provide reasonable doubt as to the accuracy of the broad statement made in support of enablement of claims. See Ex parte Singh, 17 USPQ2d 1714 (BPAI 1991). Therefore, one skill in the art would have to engage in excessive and undue amount of experimentation to exercise the invention as claimed.

Claims 26-31, 35 and 39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 26 and 27 recites limitation "a functional equivalent thereof". It is unclear what is the functional equivalent thereof in this context. The applicant argues that the specification teaches that functional portion of an LTR's U3 and R region is described as complete promoter region or fragment thereof which is responsive to Tat transactivation (response, pages 8-9). However, this is not found persuasive because it is unclear whether in the claim 26 the functional equivalent thereof refers to the retroviral particle, PRE or HIV Rev. Similarly, in claim 27 it is unclear whether the functional equivalent thereof refers to retroviral particle or PRE.

Claim 28 is indefinite because it recites claim limitation "the NS encodes a therapeutic gene". Genes are nucleic acid and nucleic acid only encodes proteins and not genes. Changing "the NS encodes a therapeutic gene" to -- the NS encodes a therapeutic gene product -- would obviate this rejection.

Claim 29 and 31 are indefinite because instant claims recite limitation "derived from". It is unclear in what way the RNA genome or response element is derived from a retrovirus. For example, providing a single element would be "derived from" as having the whole retroviral backbone or using the oncoretroviral RNA to make mono-RNA that the cell then use to make the packageable genome i.e. the oncoretroviral RNA is used as metabolite for the genome of the particle.

Claim 35 is rejected because it recite limitation "strong promoter". It is unclear what are the metes and bounds of "strong" in this context, since the "strong" is subjective terminology.

Claim 39 is indefinite because it is unclear what set of nucleic acid would to give rise to the retroviral vector particles. It is further unclear what is include or excluded in the system as claimed. In addition, claim 39 recites the limitation "the components" in line 2. There is insufficient antecedent basis for this limitation in the claim.

Claim Objections

Claim 25 is rejected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the

claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 25 and 24 are identical in scope because the PRE as claimed in base claim 24 is identical to the PRE as claimed in the dependent claim 25. The PRE as claimed in claim 24 is retroviral sequence. Similarly, the PRE as claimed in claim 25 is also responsive to a retroviral product. There is no evidence that any retroviral PRE is not responsive to the retroviral factor as claimed.

Claim 34 is rejected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The instant claim only refers back to a part of base claim 24. In so doing claim 34 can be infringed without infringing claim 24. Changing claim 34 to an independent claim by incorporating the claim limitations of claim 24 is suggested.

Claim 37 is rejected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. In instant case claim 37 is directed to subject matter excluded by claim 34 i.e. absence of the NS. The dependent claim must contain all limitations of claim they depend from. Changing claim 37 to an independent claim by incorporating the claim limitations of claim 24 and 37 is suggested.

Conclusion

Claims 25, 34 and 37 are objected.

Claims 26-31, 35 and 39 are rejected.

Claims 24, 32-33, 36, 38, 40-43 are allowed.

Claims 24, 32-33, 36, 38, 40-43 are free of prior art of record because the prior art dose not teach or suggest a retroviral particle comprising a packageable retroviral RNA genome when in the form of DNA provirus comprises a 5'LTR comprising tat inducible HIV U3 and R regions, a nucleotide sequence (NS) and polynucleotides response element (PRE), wherein the NS and PRE are located within an intron in a transcription unit of the provirus flanked by a retroviral splice donor (SD) site and splice acceptor (SA) sites derived from different retroviruses, wherein the NS expression is undetectable in cells not expressing Tat and Rev genes.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is (703) 305-6838. The examiner can normally be reached on Monday-Friday from 9:00 AM to 5:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Irem.Yucel can be reached on (703) 305-1998. The fax-phone number for the organization where this application or proceeding is assigned as (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the patent analyst Zeta Adams, whose telephone number is (703) 305-3291.

S. Kaushal
Patent examiner

SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER